Q4 35. (Amended) A primer set for amplifying a polynucleotide encoding the polypeptide of SEQ ID NO:1 comprising a polyT/Not reverse primer and SEQ ID NO:10 as a forward primer.

36. (Amended) A kit for amplifying and/or detecting a polypeptide or fragment thereof encoding the polypeptide of SEQ ID NO:1 comprising at least one primer selected from the group consisting of SEQ ID NOs:8, 9, and 10.

Concluded

REMARKS

We thank the Examiner and his supervisor (Dr. Ponnathapura Achutamurthy) for the courtesies extended during a series of teleconferences with the undersigned and Gonzalo Merino of our office during the pendency of the present Office Action (Paper No. 8). We briefly summarize below the content of these teleconferences.

The undersigned brought to the Examiners' attention the realization by the Applicants that the function of the enzyme represented by SEQ ID NO:1 was misidentified in the specification. In particular, the undersigned explained to the Examiners that the enzyme represented by the polypeptide sequence of SEQ ID NO:1 was identified in the specification as a ***di***oxygenase (*i.e.*, a β,β-carotene 15, 15-***di***oxygenase). Subsequent studies that were sensitive enough to detect symmetric versus non-symmetric metabolites of β,β-carotene revealed that the enzyme identified in the instant application is a β,β-carotene 15,15'-***mono***oxygenase, rather than a β,β-carotene 15,15'-***di***oxygenase. All other physical and structural properties of the enzyme identified in the instant application have remained unchanged.

Moreover, the specification clearly identifies the utility of the claimed polypeptide designated by SEQ ID NO:1 (and its corresponding polynucleotide sequence, SEQ ID NO:2) as a participant in the pathway leading to the production of vitamin A. (*See e.g.* Page 7, lines 15-17 ("It is an object of the present invention to provide a protein having the vitamin A producing activity of β,β-carotene 15,15'-dioxygenase comprising an amino acid sequence which is identical or homologous to SEQ ID NO:1 ...."); Page 11, lines 18-19 ("The carotene can be conveniently cleaved enzymatically by using a protein of the present invention."); Page 12, lines 6-12 ("The vector having the gene and the other required genetic structures is then introduced into suitable host cells by well-known methods like transformation, transfection, electroporation or microprojectile bombardment. Depending on the thost cell it may be preferred to stably integrate the gene coding for a protein of the present invention into the genome of the host cell. The cells obtained by such methods can then be further propagated and if the cell is a plant cell it si possible to generate therefrom transgenic plants."). Thus, various utilities are disclosed in the specification for the protein of the present invention including production of vitamin A, cleavage of carotene molecules, and the production of transgenic plants. Any one of these asserted utilities is sufficient to meet the statutory requirements under 35 U.S.C. §101.

In view of the foregoing, the recitation of "β,β-carotene 15,15'-dioxygenase" in claims 14, 15, 19, 20, 27, 28, and 34-36 and of "β,β-carotene 15,15'-dioxygenase activity" in claims 12 and 13, has been replaced with the recitation "a polypeptide having the function of the polypeptide represented by SEQ ID NO:1." Because the name (*i.e.*, function) of the enzyme is an inherent property of the enzyme correctly identified by SEQ ID NO:1, the above-identified amendments do not constitute new matter. (*See* MPEP §2163.07(a) at 2100-128 ed. 7 rev. 1

(Feb. 2000); *In re Papesch*, 137 USPQ 43, 51 (C.C.P.A. 1963) ("From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing."); *In re Kirchner*, 134 USPQ 324, 329 (C.C.P.A. 1962) "Always lurking in the background of the argument of the Patent Office is an echo of a theory which was initially propounded by the examiner but never really pursued before us, namely, that 'the invention' in the case of a new chemical compound is not the compound itself ... but is a compound coupled with a disclosed use ...We think the Board of Interference Examiners gave a very good answer in the latter case (*Biel v. Coan*) when it said: Coan's view is untenable and if adopted could lead to extraordinary results."); *In re Nathan*, 140 USPQ 601, 604 (C.C.P.A. 1964) (later added limitation to the claims of a 2-halo substituent as "alpha-oriented" was an "inherent characteristic" of the claimed subject matter); and *Kennecott Corp. v. Kyocera International, Inc.* 5 USPQ2d 1194, 1198 (Fed. Cir. 1987) ("The disclosure in a subsequent patent application of an inherent property of a product does not deprive that product of the benefit of an earlier filing date. Nor does the inclusion of a description of that property in later-filed claims change this reasonable result.").

Claim 6 has been amended to recite "[a]n isolated nucleic acid sequence encoding a polypeptide of SEQ ID NO: 1." Support for this amendment is found in original claims 1 and 6, and in the specification at, for example, page 1, lines 24-31. *See*, *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claim 8 has been amended to recite "[a]n isolated nucleic acid sequence comprising at least 20 bases of SEQ ID NO: 2 or at least 20 bases of the nucleic acid sequence that encodes SEQ ID NO:1.." Support for this amendment is found in original claim 8 and in the specification at, for example, page 9, lines 4-9. (*Id.*).

Claim 9 has been amended to recite "[a]n isolated nucleic acid sequence comprising at least 30 bases of SEQ ID NO:2 or at least 30 bases of the nucleic acid sequence that encodes SEQ ID NO:1." Support for this amendment is found in original claim 9 and in the specification at, for example, page 9, lines 4-9. (*Id.*).

Claim 11 has been amended to recite "[a]n isolated nucleic acid sequence comprising an antisense ribonucleic acid, which binds to the nucleic acid sequence according to claim 6." Support for this amendment is found in original claim 11 and in the specification at, for example, page 9, lines 14-26. (*Id.*).

Claims 12-15, 19, 27, 28, and 34-36 have been amended by replacing the recitation of "a polypeptide having β,β-carotene 15,15'-dioxygenase activity" or "β,β-carotene 15,15'-dioxygenase" with --the polypeptide of SEQ ID NO:1--. Support for these amendments is found in the specification at, for example, Figure 4 and page 1, lines 24-25.

Claim 19 also has been amended to remove its dependence on claim 1. Support for this amendment is found in original claims 1 and 19. (*Id.*).

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Restriction Requirement

The election to prosecute the subject matter of Group II (claims 6-15, 19-32, and 34-36) is hereby affirmed.

Objections to the Claims

Claims 6 and 19 were objected to "as being dependent upon a non-elected base claim." (Paper 8 at 6). With a view towards furthering prosecution, claims 6 and 19 have been amended to remove their dependence on claim 1. Accordingly, it respectfully is submitted that the objections are rendered moot and should be withdrawn.

Claims 8 and 9 were objected to under 37 C.F.R. 1.75(c), "as being of improper dependent form for failing to further limit the subject matter of a previous claim." (*Id.*). The Examiner further stated that claims 8 and 9 "do not include the limitation of the claim on which it depends because a DNA of 20 bases cannot encode a polypeptide that is more than 60% identical to SEQ ID NO:1." (*Id.*).

With a view towards furthering prosecution, claims 8 and 9 have been amended to remove their dependency on claim 6 and to remove any recitation of "homology" or "identity." In view of the foregoing, it respectfully is submitted that the objections are rendered moot and should be withdrawn.

§112, Second Paragraph

Claims 8, 9, and 11 were rejected under 35 U.S.C. §112, second paragraph. (Paper No. 8 at 9). In making the rejection, the Examiner asserted that fragments of 20 and 30 base pairs, as recited by claims 8 and 9 respectively, "are unclear because ... [the fragments] cannot encode an enzyme that is more than 60% identical to SEQ ID NO:1." (Paper 8 at 9-10).

With a view toward furthering prosecution, claims 8 and 9 have been amended to remove the % identity limitation. Accordingly, it respectfully is submitted that the rejection is rendered moot and should be withdrawn.

The Examiner further asserted that claim 11 is "unclear because an antisense by definition does not encode a polypeptide but is complimentary to a mRNA of a polypeptide." (Paper 8 at 10). With a view towards furthering prosecution, claim 11 has been amended to clarify that the nucleic acid sequence is "an antisense ribonucleic acid, which binds to the nucleic acid sequence according to claim 6." In view of this amendment, it respectfully is submitted that this rejection is also rendered moot and should be withdrawn.

§112, First Paragraph

Claims 8 and 9 were rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (Paper 8 at 6). In making the rejection, the Examiner asserted that "[a]pplicants fail to describe any representative species by identifying characteristics or structural properties other than the functionality of being a β,β-carotene 15,15'-dioxygenase oxidase." (*Id.* at 7).

With a view towards furthering prosecution, claims 8 and 9 have been amended to remove any recitation of a "%homology" or "%identity" limitation. As amended, claims 8 and 9 are clearly tied to either SEQ ID NO:2 or a nucleic acid encoding SEQ ID NO:1, both of which structures are fully disclosed in the specification.

Moreover, nucleotide sequences of the claimed sizes, are also disclosed in the specification. (*See e.g.,* page 9, lines 4-9). Furthermore, the specification discloses that nucleic acid fragments for use in PCR may be selected from regions that are highly conserved within the

encoded protein. (*See e.g.* page 9, lines 7-9 and 19-30). And, a representative number of peptides and nucleic acid sequences within the scope of claims 8 and 9 are disclosed in the specification. (*See e.g.* Examples 3 and 4 and SEQ ID NOs:3 and 6-10). Accordingly, it is respectfully submitted that it would be readily apparent that applicants were in possession of the invention at the time the application was filed. For these reasons, withdrawal of the rejection respectfully is requested.

Claims 6-15 and 19-27 were rejected under 35 U.S.C. §112, first paragraph. (Paper No. 8 at 7). In making the rejection, the Examiner acknowledged that the specification is enabled for DNA molecules encoding SEQ ID NO:1. The Examiner, however, asserted that the specification "does not reasonably provide enablement for any DNA or DNA fragments encoding a β,β-carotene 15,15'-dioxygenase having 60% homology to SEQ ID NO:1 or comprising 20 or 30 bases of SEQ ID NO:2." (*Id.*). The Examiner further asserted that "the breadth of these claims is much larger than the scope enable [sic] by the specification" because "applicants do not teach which 60% of SEQ ID NO:1 must be retained and which 40% of SEQ ID NO:1 can be modified" and still obtain a functional enzyme. (*Id.* at 8). The Examiner also asserted that "it is unpredictable whether a DNA fragment comprising 20 or 30 bases ... encodes a functional enzyme." (*Id.*).

In view of the amendment to claims 6, 8, 9, and 19, none of rejected claims 6-15 and 19-27 recite a "homology" or "identity" element. Accordingly, it respectfully is submitted that the portion of the rejection regarding polypeptides "having 60% homology" has been rendered moot and should be withdrawn.

With respect to the Examiner's comments regarding 20 or 30 bases of SEQ ID NO:2, we note that the specification provides ample guidance regarding the generation of fragments of the recited sizes. *See e.g.* page 9, lines 5-9 and 19-26, and Example 4. Moreover, as noted above, representative peptide fragments and PCR primers are disclosed in Examples 3 and 4, respectively. Accordingly, the specification enables the full scope of the amended claims, and consequently, the rejection should be withdrawn.

In view of the foregoing, favorable action on the merits including entry of the amendments, withdrawal of the rejections, and allowance of all the claims, respectfully, is requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, DC 20231, on July 31, 2001.

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Respectfully submitted,

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"Marked Up" Amendments to Claims Pursuant to Rule 1.121(c)

6. (Amended) An isolated nucleic acid sequence encoding a polypeptide of SEQ ID NO: 1 [the polypeptide of claim 1].

8. (Amended) An isolated nucleic acid sequence comprising at least 20 bases of SEQ ID NO: 2 or at least 20 bases of the nucleic acid sequence that encodes SEQ ID NO:1 [according to claim 7 wherein the fragment has at least 20 bases].

9. (Amended) An isolated nucleic acid sequence comprising at least 30 bases of SEQ ID NO:2 or at least 30 bases of the nucleic acid sequence that encodes SEQ ID NO:1 [according to claim 7 wherein the fragment has at least 30 bases].

11. (Amended) An isolated nucleic acid sequence comprising an antisense ribonucleic acid, which binds to the nucleic acid sequence according to claim 6 [wherein the nucleic acid is an antisense ribonucleic acid].

12. (Amended) A primer for amplifying a gene coding for the polypeptide of SEQ ID NO: 1 [a polypeptide having β,β-carotene 15,15'-dioxygenase activity] which primer comprises a fragment of the nucleic acid sequence according to claim 6.

13. (Amended) A probe for detecting a gene coding for the polypeptide of SEQ ID NO: 1 [a polypeptide having β,β-carotene 15,15'-dioxygenase activity] which probe comprises a fragment of the nucleic acid sequence according to claim 6.

14. (Amended) A test kit for amplifying and/or detecting a gene or a fragment thereof coding for the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] wherein the test kit comprises at least one primer according to claim 12.

15. (Amended) A test kit for amplifying and/or detecting a gene or a fragment thereof coding for the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] wherein the test kit comprises at least one probe according to claim 13.

19. (Amended) A method for introducing a [β,β-carotene 15,15'-dioxygenase] cDNA coding for the polypeptide of SEQ ID NO: 1 into a host cell comprising introducing a cDNA coding for the polypeptide of SEQ ID NO: 1 [the polypeptide of claim 1] into a vector suitable for the host cell and introducing the vector into the host cell.

27. (Amended) A host cell according to claim 26 which comprises a [β,β-carotene 15,15'-dioxygenase] cDNA coding for the polypeptide of SEQ ID NO: 1 obtained from another species.

28. (Amended) An isolated polynucleotide which encodes the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] comprising SEQ ID NO: 2.

34. (Amended) A primer set for amplifying a polynucleotide encoding the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] comprising SEQ ID NO: 8 as a 5' primer and SEQ ID NO: 9 as a 3' primer.

35. (Amended) A primer set for amplifying a polynucleotide encoding the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] comprising a polyT/Not reverse primer and SEQ ID NO: 10 as a forward primer.

36. (Amended) A kit for amplifying and/or detecting a polypeptide or fragment thereof encoding the polypeptide of SEQ ID NO: 1 [β,β-carotene 15,15'-dioxygenase] comprising at least one primer selected from the group consisting of SEQ ID Nos: 8, 9, and 10.